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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,843	08/04/2003	C. Frank Bennett	RTS-0242US.C1	5669

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/633,843	BENNETT ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10 and 12-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,12 and 14* is/are rejected.

7)☒ Claim(s) *6-10 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *October 3, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *sequence alignment*.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed February 10, 2006.

Claims 11 and 15 have been canceled. Claim 1 has been amended.

Claims 1, 2, 4-10, and 12-14 are pending in the instant application.

Claims 1, 2, 4-10, and 12-14 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

Applicant's information disclosure statement filed August 11, 2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Claim Rejections - 35 USC § 112

In the previous Office Action mailed November 15, 2005, claim 11 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This rejection is moot** in view of Applicant's Amendment to cancel claim 11 in the Amendment filed February 10, 2006.

In the previous Office Action mailed November 15, 2005, claim 15 was rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of *in vitro* (cell culture) inhibition of superoxide dismutase 1 soluble in cells or tissues comprising administering an antisense compound targeted to the coding region of a nucleic acid molecule encoding superoxide dismutase 1 soluble, does not reasonably provide enablement for *in vivo* (whole organism) inhibition of superoxide dismutase 1 soluble in cells or tissues comprising administering an antisense compound targeted to a coding region of a nucleic acid molecule encoding superoxide dismutase 1 soluble. **This rejection is moot** in view of Applicant's Amendment to cancel claim 15 in the Amendment filed February 10, 2006.

Claim Rejections - 35 USC § 102

In the previous Office Action mailed November 15, 2005, claims 1, 2, 4, 5, 11, and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Rothstein et al. (Proc. Natl. Acad. Sci., 1994 Vol. 91:4155-4159, reference AK on Applicant's information disclosure statement filed August 4, 2003). **This rejection is moot** against claims 11 and 15 in view of Applicant's Amendment to cancel these claims in the Amendment filed February 10, 2006. **This rejection is withdrawn** against claims 1, 2, 4, and 5 in view of Applicant's Amendment to the claims filed February 10, 2006. Specifically, the Examiner is withdrawing these rejections in view of Applicant's Amendment to claim 1 to recite "wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NO:13 or SEQ ID NO:15".

Claim Rejections - 35 USC § 103

In the previous Office Action mailed November 15, 2005, claims 1, 2, and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothstein et al. (Proc. Natl. Acad. Sci., 1994 Vol. 91:4155-4159, reference AK on Applicant's information disclosure statement filed August 4, 2003) in view of Baracchini et al. [U.S. Patent No. 5,801,154]. **This rejection is moot** against claims 11 and 15 in view of Applicant's Amendment to cancel these claims in the Amendment filed February 10, 2006. **This rejection is withdrawn** against claims 1, 2, 4, and 5 in view of Applicant's Amendment to the claims filed February 10, 2006. Specifically, the Examiner is withdrawing these rejections in view of Applicant's Amendment to claim 1 to recite "wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NO:13 or SEQ ID NO:15".

Applicant's Amendment necessitated the new grounds of rejection presented below:

Claim Objections

Claims 1, 2, 4-10, and 12-14 are objected to because of the following informalities: Claim 1 contains a typographical error since it appears that the word "nuclebase" is incorrectly spelled and should be correctly spelled as "nucleobase". Appropriate correction is required. Claims 2, 4-10, and 12-14 are objected to because they are dependent therein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 12, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Rossau et al. [U.S. Patent No. 5,536,638] ('638).

Claim 1 is drawn to a compound 8 to 50 nucleobases in length targeted to a coding region of a nucleic acid molecule encoding human superoxide dismutase 1, soluble (SEQ ID NO:3), wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NO:13 or SEQ ID NO:15. Claim 2 depends from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide. Claims 12 and 14 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound of claim 1 further comprises a composition comprising a pharmaceutical acceptable carrier or diluent and wherein the composition is an antisense oligonucleotide.

Rossau et al., '638 discloses primer pairs which can be used in PCR reactions for the amplification of fragments spanning the spacer region between the 16S and 23S rRNA genes. Specifically, '638 discloses a primer with the following sequence:

5'-cacgtccttcgtcgcct-3' (see SEQ ID NO:102). It is noted that SEQ ID NO:102 disclosed by Rossau et al. binds to the last 10-nucleobase portion of SEQ ID NO:13 (see attached sequence alignment). It is noted that since the primer pairs disclosed by

Rossau et al., '638 are used in PCR reactions, the water or buffers contained in the PCR mixture constitute as pharmaceutically acceptable carrier(s) as claimed.

The burden of establishing whether the prior art primer has the further function of functioning as an antisense oligonucleotide under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence that the primer disclosed by Rossau et al., '638 would or would not have the additional functional limitation of performing as an antisense oligonucleotide.

Therefore, absent evidence to the contrary, claims 1, 2, 12, and 14 are anticipated by Rossau et al., '638.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossau et al. [U.S. Patent No. 5,536,638] ('638) in view of Skerra, A. (Nucleic Acids Research, 1992 Vol. 20:3551-3554).

Claim 1 is drawn to a compound 8 to 50 nucleobases in length targeted to a coding region of a nucleic acid molecule encoding human superoxide dismutase 1, soluble (SEQ ID NO:3), wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NO:13 or SEQ ID NO:15. Claim 2, 4, and 5 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide; wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage; and wherein the modified internucleoside linkage is a phosphorothioate linkage. Claims 12 and 14 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound of claim 1 further comprises a composition comprising a pharmaceutical acceptable carrier or diluent and wherein the composition is an antisense oligonucleotide.

Rossau et al., '638 discloses primer pairs which can be used in PCR reactions for the amplification of fragments spanning the spacer region between the 16S and 23S rRNA genes. Specifically, '638 discloses a primer with the following sequence:

5'-cacgtccttcgtcgcct-3' (see SEQ ID NO:102). It is noted that SEQ ID NO:102 disclosed by Rossau et al. binds to the last 10-nucleobase portion of SEQ ID NO:13 (see attached sequence alignment). It is noted that since the primer pairs disclosed by Rossau et al., '638 are used in PCR reactions, the water or buffers contained in the PCR mixture constitute as pharmaceutically acceptable carrier(s) as claimed.

The burden of establishing whether the prior art primer has the further function of functioning as an antisense oligonucleotide under generally any assay conditions falls to Applicant. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See also MPEP 2112: "[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product." The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above. Therefore, it falls to Applicant to determine and provide evidence

that the primer disclosed by Rossau et al., '638 would or would not have the additional functional limitation of performing as an antisense oligonucleotide.

Rossau et al., '638 do not teach a compound comprising at least one modified internucleoside linkage, wherein the modified internucleoside linkage is a phosphorothioate linkage.

Skerra teach phosphorothioate primers improve the amplification of DNA sequences by DNA polymerases with proofreading activity (see Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to make compound targeted to a coding region of a nucleic acid molecule encoding human superoxide dismutase 1, soluble (SEQ ID NO:3), wherein said compound comprises at least an 8-nucleobase portion of SEQ ID NO:13 using the teachings of Rossau et al. One of ordinary skill in the art would have been motivated to have the primer comprise modified internucleoside linkage since Skerra teach phosphorothioate primers improve the amplification of DNA sequences by DNA polymerases with proofreading activity during PCR. One of ordinary skill in the art would have expected success at incorporating a modified internucleoside linkage on the primer since it is routine in the art to modify nucleic acids to include non-naturally occurring backbone linkages, including phosphorothioate linkages, to increase resistance to nuclease attack and since Skerra explicitly taught the successful design and use of phosphorothioate primers in PCR analysis.

Therefore, absent evidence to the contrary, claims 11, 2, 4, 5, 12, and 14 would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention

was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
March 27, 2006

SEAN McGARRY
PRIMARY EXAMINER
AU 1635

Sequence alignment

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RESULT 5
I23680/c
LOCUS       I23680                   17 bp    DNA     linear   PAT 07-OCT-1996
DEFINITION  Sequence 102 from patent US 5536638.
ACCESSION   I23680
VERSION     I23680.1  GI:1603550
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 17)
  AUTHORS   Rossau,R. and Van Heuverswyn,H.
  TITLE     Hybridization probes derived from the spacer region between the 16S
            and 23S rRNA genes for the detection of Neisseria gonorrhoeae
  JOURNAL   Patent: US 5536638-A 102 16-JUL-1996;
FEATURES             Location/Qualifiers
     source          1..17
                     /organism="unknown"
                     /mol_type="unassigned DNA"

  Query Match          40.0%;  Score 14.4;  DB 1;  Length 17;
  Best Local Similarity  93.8%;  Pred. No. 6.3;
  Matches   15;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          3 GGCGACGAAGGCCGTG 18
              ||||||||||| ||||
Db         16 GGCGACGAAGGACGTG 1
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